Computational study of the risk of restenosis in coronary artery bypass grafts

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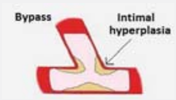
Clinical problem

Coronary artery disease is caused by the buildup of atherosclerotic plaques in the coronary vessel walls

→ Reduction of oxygen supply to the heart, leading to ischemia, ventricular fibrillation and heart failure

Surgical treatment: coronary artery bypass graft

Possible complication: bypasses in patients with non-severe stenosis (<70%) may fail due to anastomotic restenosis [1]



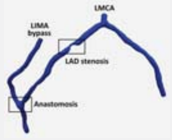
Objective
We look for a possible **relationship between stenosis degree and risk of graft failure** in terms of WSS-based hemodynamic indices potentially involved in *intimal hyperplasia* development

Materials and Methods

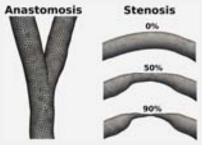
From CT scans to computational domains

With software VMTK (www.vmtk.org):

- Level-set segmentation to reconstruct the *patient-specific geometries*
- Ad-hoc scripts to *virtually change the degree of coronary stenosis*
- Surfaces turned into *volumetric meshes of tetrahedra*



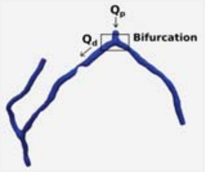
LMCA = Left main coronary artery
LIMA = Left interior mammay artery
LAD = Left anterior descending



Extension of Murray's law

In order to prescribe *realistic boundary conditions* in our numerical simulations, we need to estimate the *flow division* at bifurcations

Murray's law [2]: $\frac{Q_d}{Q_p} = \left(\frac{r_d}{r_p}\right)^3$, $d = \text{daughter}, \ p = \text{parent}$



However, Murray's law is valid only for healthy vessels and Newtonian fluids

→ We propose an **extended Murray's law** to account for:
- presence of a stenosis in the daughter vessel
- non-Newtonian rheology of blood

Extended Murray's law:

$$\frac{Q_d}{Q_p} = \frac{Q^{sten}(r_d, \alpha, \mu_{1,d}, \mu_{2,d}, \mu_{3,d}, l_{1,d}, l_{2,d}, l_{3,d})}{\sqrt{\frac{\pi^2 m}{16\mu_p}}\, r_p^3}$$

for a suitable function Q^{sten} *

Stenosis schematization

* see [3] for more details about the expression of Q^{sten} and its derivation

If the daughter vessel is not stenotic (*α = 1*) → $\frac{Q_d}{Q_p} = \sqrt{\frac{\mu_p}{\mu_d}}\left(\frac{r_d}{r_p}\right)^3$

N.B. In case of Newtonian flow ($\mu_p = \mu_d$), the original Murray's law is recovered

Governing equations and boundary conditions

Discretized-in-time Navier-Stokes equations:

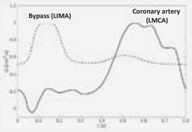
$$\begin{cases} \rho_f \frac{\mathbf{u}^n - \mathbf{u}^{n-1}}{\Delta t} + \rho_f \mathbf{u}^{n-1} \cdot \nabla \mathbf{u}^n - \nabla \cdot \left[\mu(\mathbf{u}^{n-1})\left(\nabla \mathbf{u}^n + (\nabla \mathbf{u}^n)^T\right)\right] + \nabla p^n = \mathbf{0} \\ \nabla \cdot \mathbf{u}^n = 0 \end{cases}$$

- *Shear-thinning* behavior of blood described by **Carreau-Yasuda** model [4]:

$$\mu(\mathbf{x}, t) = \mu_\infty + (\mu_0 - \mu_\infty)\left(1 + (\lambda\dot{\gamma}(\mathbf{x}, t))^a\right)^{\frac{n-1}{a}}$$

- Semi-implicit treatment of convective and diffusive terms
- Equations numerically approximated and solved with the *Finite Element library LifeV*** (www.lifev.org)

**developed at MOX - Politecnico di Milano, INRIA – Paris, CMCS – EPF de Lausanne, Emory University - Atlanta



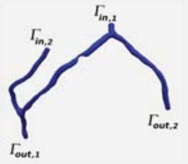
Patient-specific velocity/pressure data unavailable

→ We chose from literature **representative flow rate waveforms** for the coronary artery and bypass inlets

For the LIMA bypass, the amplitude of the signal is set in accordance to the stenosis degree, in order to guarantee that the **flow rate perfusing the myocardium** (calibrated by means of a *healthy* simulation) **remains constant**, as observed in the clinical practice [1] (see [3] for more details)

→ At each time t^n, we solve the NS equations with the following BCs:

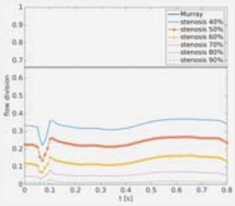
- Flow rate condition at $\Gamma_{in,1}$: $\int_{\Gamma_{in,1}} \boldsymbol{u}^n \cdot \boldsymbol{n}\, d\gamma = Q_{LMCA}(t^n)$
- Flow rate condition at $\Gamma_{in,2}$: $\int_{\Gamma_{in,2}} \boldsymbol{u}^n \cdot \boldsymbol{n}\, d\gamma = Q^X_{LIMA}(t^n)$
- Flow rate condition at $\Gamma_{out,1}$: $\int_{\Gamma_{out,1}} \boldsymbol{u}^n \cdot \boldsymbol{n}\, d\gamma = Q^X_{LIMA}(t^n) + Q^X_{LAD}(t^n)$
- Zero-traction condition at $\Gamma_{out,2}$: $-p^n \boldsymbol{n} + \mu(\boldsymbol{u}^{n-1})\left(\nabla \boldsymbol{u}^n + (\nabla \boldsymbol{u}^n)^T\right)\boldsymbol{n} = 0$



Flow rate conditions are imposed with a **Lagrange multipliers** approach [5]

Results

Flow divisions with different stenosis degree



- The original Murray's law overestimates the flow division with respect to our extension
- The proposed extended Murray's law detects different degrees of stenosis, providing decreasing flow divisions for increasing stenosis degree

Risk of anastomotic restenosis

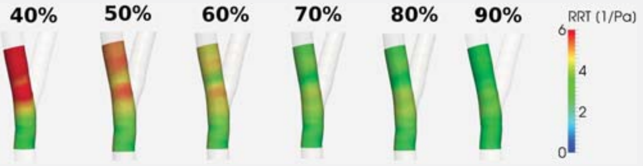
- The *Relative Residence Time* (RRT) is related to intimal hyperplasia development

$$RRT(\boldsymbol{x}) = \frac{1}{(1 - 2OSI(\boldsymbol{x}))TAWSS(\boldsymbol{x})}$$

$$OSI(\boldsymbol{x}) = \frac{1}{2}\left(1 - \frac{\left\|\int_0^T \boldsymbol{\tau}_w(t, \boldsymbol{x})dt\right\|}{\int_0^T \|\boldsymbol{\tau}_w(t, \boldsymbol{x})\|\, dt}\right)$$

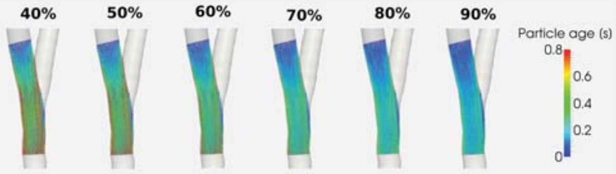
$$TAWSS(\boldsymbol{x}) = \frac{1}{T}\int_0^T \|\boldsymbol{\tau}_w(t, \boldsymbol{x})\|\, dt$$

$\boldsymbol{\tau}_w =$ *Wall Shear Stess*



→ The lower the degree of stenosis, the higher the RRT and thus the higher the risk of anastomotic restenosis (graft failure)

- *Particle tracking techniques* allow to follow particles and to quantify the *residence time* spent by each particle inside a region of interest



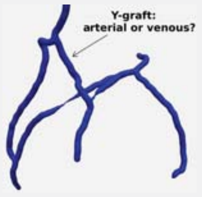
→ Stagnation regions are more likely to occur in cases with non-severe stenosis (longer particle ages), possibly enhancing the risk of restenosis

Conclusions and future perspectives

- The extended Murray's law may be a suitable alternative to the prescription of realistic BCs when clinical data are not available
- Lower LAD stenosis degrees result in higher RRT values and longer residence times, possibly enhancing the risk of LIMA graft restenosis

Future developments:

- *Validation* of the extended Murray's law
- *Fluid-structure interaction* (FSI) modeling of the coronary tree with multiple bypasses (Y-grafts)



→ Analyze the influence of the type of bypass (arterial or venous) on the risk of anastomotic restenosis due to compliance mismatch

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